UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND
GREENBELT DIVISION

MALLINCKRODT INC.,
675 McDonnell Boulevard
Hazelwood, MO 63042,

Plaintiff,

vs.

UNITED STATES FOOD AND DRUG ADMINISTRATION,
Montgomery County,
10903 New Hampshire Avenue
Silver Spring, MD 20993

and

UNITED STATES OF AMERICA,
c/o Office of the United States Attorney for the District of Maryland,
Prince George's County,
6406 Ivy Lane, Suite 800
Greenbelt, MD 20770,

Defendants.

C.A. No. _____

COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

Plaintiff Mallinckrodt Inc. hereby brings this action for judicial review of actions by the United States Food and Drug Administration ("FDA") regarding Plaintiff's methylphenidate hydrochloride extended-release tablets, a generic version of the brand product Concerta®. These actions have harmed Plaintiff and will continue to do so until

this Court intervenes. The Court should issue a declaratory judgment holding that FDA's actions are unlawful and issue a permanent injunction setting those actions aside and otherwise prohibiting FDA from effectuating them in the future without following applicable legal requirements.

Jurisdiction and Venue

1. This Court has jurisdiction over this action under 28 U.S.C. § 1331, to provide remedies set forth in 5 U.S.C. § 706 and 28 U.S.C. § 2201.

2. Venue is proper in this District under 28 U.S.C. § 1391(e).

Parties

3. Plaintiff Mallinckrodt Inc. ("Mallinckrodt") is a pharmaceutical manufacturer incorporated under the laws of Delaware, with its U.S. headquarters at 675 McDonnell Blvd., Hazelwood, Missouri.

4. Defendant FDA has regulatory authority over the drug at issue in this case and has taken the adverse actions challenged in this Complaint. Defendant United States of America is named as a defendant pursuant to 5 U.S.C. §§ 702-703, because this is an action for judicial review of actions of an agency of the United States that have affected Plaintiff adversely.

Statutory and Regulatory Background

5. The regulatory regime governing FDA's authority for premarket approval of drugs is set forth in the Federal Food, Drug, and Cosmetic Act ("FFDCA"), 21 U.S.C.

§ 301 *et seq*. The FFDCA applies separate requirements for the approval of new brand-name drugs (also known as innovator drugs) and generic drugs. Although the process of approving brand-name drugs is typically more burdensome and time-consuming, prior to approval of both types of drugs, FDA must conduct an extensive review to determine that the drug is safe and effective.

6. In order to market and sell a brand-name drug, a company must submit a New Drug Application ("NDA"). As set forth in 21 U.S.C. § 355, an NDA must outline and explain the drug's ingredients, the results of clinical tests, the results of animal studies, how the drug behaves in the body, and how the drug is manufactured, processed, and packaged. Before approving an NDA, FDA must evaluate numerous statutorily-defined criteria, including whether the drug is safe and effective in its proposed use. *See* 21 U.S.C. § 355 *et seq*.

7. In order to market and sell a generic drug, a company must submit an Abbreviated New Drug Application ("ANDA"). As set forth in 21 U.S.C. § 355(j), an ANDA applicant may obtain FDA approval of a drug that is the "same" as a previously approved brand-name drug without conducting the full battery of clinical and non-clinical studies that are required for an NDA. *See generally* 21 U.S.C. § 355(j).

8. An ANDA applicant is allowed to rely upon a prior FDA finding of safety and efficacy for the approved brand-name drug that is referenced by the ANDA applicant, provided that the proposed generic drug is the "same" as the approved brand-

name drug with regard to active ingredients, dosage form, route of administration, strength, and labeling. *Id*. § 355(j)(2)(A)(i), (ii), (iii), and (v).

9. In addition, before approving an ANDA, FDA is required to determine that the proposed generic drug is "bioequivalent" to the referenced brand-name drug. *See* 21 U.S.C. § 355(j)(4)(F); 21 C.F.R. § 314.127(a)(6)(i). In general, a generic drug is "bioequivalent" to the corresponding brand-name drug if, in single-dose or multiple dose clinical studies, the "rate and extent of absorption" of the two drugs are not significantly different. *See* 21 U.S.C. § 355(j)(8)(B).

10. The FFDCA mandates that FDA publish a list of approved drugs with therapeutic equivalence information. *See* 21 U.S.C. § 355(j)(7)(A)(i)(I)-(III). FDA has elected to fulfill this statutory duty by publishing the *Approved Drug Products with Therapeutic Equivalence Evaluations*, commonly known as the "Orange Book."

11. The Orange Book contains FDA's therapeutic equivalence evaluations, which are presented in the form of two-letter codes that indicate the basis for the evaluation made (e.g., AA, AB, BP, BX). According to the Orange Book's preface, these therapeutic evaluations "have been prepared to serve as public information and advice to state health agencies, prescribers, and pharmacists to promote public education in the area of drug product selection and to foster containment of health care costs."

12. The Orange Book provides an explanation of the specific therapeutic equivalence two-letter codes. Relevant here, FDA uses various "A codes" and "B codes"

to designate whether the drug product is considered by FDA to be therapeutically equivalent to another listed drug. Those drugs considered by FDA to be therapeutically equivalent are listed with a two-letter code beginning with "A." Those drugs not considered by FDA to be therapeutically equivalent are listed with a two-letter code beginning with "B."

13. It is well understood by FDA and industry that these Orange Book evaluations are the recognized standard throughout the United States for determining whether a pharmacist may substitute one drug for another. Under various state regulatory mechanisms, for example, pharmacists cannot lawfully fill prescriptions for brand drugs with generic drugs listed with a "B code." Thus, FDA's designation of a generic drug with a "B code" effectively renders the drug unsellable and unmarketable.

14. Once an ANDA is approved, FDA is authorized to take a drug off the market only through a statutorily-mandated process, as defined in 21 U.S.C. § 355(e). Section 355(e) requires "due notice and opportunity for hearing to the applicant."

15. There is no statutory mechanism by which FDA can lawfully take a generic drug off the market without providing the applicant notice and an opportunity for a hearing.

16. FDA is required by law to provide the applicant notice and an opportunity for a hearing even in those instances in which FDA believes there is an imminent health risk. The statute requires FDA to allow the applicant an opportunity for an "expedited

hearing" in the event the Secretary finds there is "an imminent hazard to the public health." FDA has expressly acknowledged that no such safety risk is at issue here.

The Parties' Dispute

17. Mallinckrodt markets and sells methylphenidate hydrochloride extended-release tablets, in 27 mg, 36 mg, and 54 mg strengths ("methylphenidate ER tablets") used to treat patients suffering from attention-deficit hyperactivity disorder.

18. On or about December 30, 2010, Mallinckrodt filed with FDA an ANDA to demonstrate that Mallinckrodt's methylphenidate ER tablets are a safe and effective generic substitute for brand drug Concerta® Extended-Release tablets. FDA designated this application as ANDA 202608.

19. On or about July 19, 2012, FDA issued new biostudy requirements for ANDAs that referenced the Concerta® drug. Subsequently, on or about September 14, 2012, FDA published new draft biostudy recommendations for methylphenidate ER tablets. *See* 77 Fed. Reg. 56,851 (Sept. 14, 2012). In its ANDA 202608, Mallinckrodt submitted a scientific biostudy that satisfied FDA's 2012 guidance.

20. On or about December 28, 2012, FDA approved ANDA 202608. FDA's approval letter states: "We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling." FDA's approval letter also states that FDA had determined that Mallinckrodt's methylphenidate ER tablets "to be bioequivalent and, therefore, therapeutically equivalent to the reference-listed drug

(RLD), Concerta Extended-Release tablets, 27 mg, 36 mg, and 54 mg, respectively, of Janssen Pharmaceuticals, Inc. (Janssen)."

21. Based on FDA's approval, FDA listed the methylphenidate ER tablets as "AB" rated in the "Orange Book." As explained in the Orange Book, the "AB" designation is a "Therapeutic Equivalence (TE)" code signifying that "a drug company's approved application contains adequate scientific evidence establishing through *in vivo* and/or *in vitro* studies the bioequivalence of the product to a selected reference listed drug." *See* http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm.

22. In December 2012, based on FDA's approval, Mallinckrodt launched its methylphenidate ER tablets as the first generic alternative to Concerta®. Since that time, Mallinckrodt's methylphenidate ER tablets have provided a cost-effective alternative to hundreds of thousands of patients.

23. Since the time that FDA approved Mallinckrodt's methylphenidate ER tablets, there has been no change in the ingredients or formulation of those tablets. The methylphenidate ER tablets that Mallinckrodt is selling today are the same as the tablets that FDA approved in December 2012.

24. Mallinckrodt's methylphenidate ER tablets are an extremely popular and successful product. Mallinckrodt supplies methylphenidate ER tablets that are dispensed through tens of thousands of pharmacies, including leading national drug stores.

Mallinckrodt's methylphenidate ER tablets have been used to fill prescriptions for patients throughout the United States.

25. Mallinckrodt sells its methylphenidate ER tablets to many customers, including retail drug store chains, large wholesale distributors, and the federal government. More than 88 million doses of Mallinckrodt's methylphenidate ER have been prescribed, with only 68 confirmed adverse events related to a lack of efficacy when the patient switched from Concerta® to Mallinckrodt's methylphenidate ER tablets. This is an extremely low reporting rate compared with overall usage of the product.

26. On November 12, 2014, FDA informed Mallinckrodt that FDA is effectuating an immediate action reclassifying Mallinckrodt's methylphenidate ER tablets from an AB rating (freely substitutable at the pharmacy level) to a BX rating (presumed to be therapeutically inequivalent).

27. FDA informed Mallinckrodt that its reclassification action was based on the application of a new "draft guidance" document regarding bioequivalence for methylphenidate hydrochloride products, even though FDA had just published that "draft guidance" on November 6, 2014, and this new draft remains open for comment through January 5, 2015.

28. Mallinckrodt objected to FDA's surprise reclassification action as not supported by appropriate evidence and not consistent with patients' best interests. Mallinckrodt also requested an opportunity to address any concerns identified by FDA,

and to engage in a dialogue with FDA. FDA, however, has not provided any opportunity for Mallinckrodt to be heard since announcing FDA's reclassification action.

29. On November 13, 2014, FDA expressly reclassified Mallinckrodt's methylphenidate ER tablets to a BX rating in the Orange Book.

30. An Orange Book rating that Mallinckrodt's methylphenidate ER tablets are therapeutically equivalent to Concerta® is essential for pharmacies to dispense this product to fill prescriptions for Concerta®. As a result of FDA's reclassification action, pharmacies will not continue to use Mallinckrodt's methylphenidate ER tablets to fill prescriptions that are written for Concerta®. FDA's reclassification action effectively takes Mallinckrodt's methylphenidate ER tablets off the market.

31. FDA's reclassification action is further unfairly harming Mallinckrodt by negatively impacting Mallinckrodt's customer relationships, Mallinckrodt's reputation for providing leading products, and Mallinckrodt's market share and competitive position.

32. Immediate relief is necessary to avoid serious and irreparable harm to Mallinckrodt as a result of FDA's sudden reclassification action.

Count I
(Agency Action Contrary to Constitutional Right or Power)

33. Plaintiff hereby incorporates by reference each and every allegation set forth in paragraphs 1 through 32 above.

34. Plaintiff's ANDA approval for methylphenidate ER tablets is a property right within the meaning of the due process clause of the Fifth Amendment to the U.S. Constitution.

35. FDA's reclassification action is a final agency action that deprives Plaintiff of a property right in the ANDA approval for methylphenidate ER tablets.

36. By failing to give Plaintiff a hearing in connection with the reclassification action, FDA has violated Plaintiff's Fifth Amendment due process right to a hearing in connection with deprivation of the property right.

37. Under 5 U.S.C. § 706(2)(B), this Court should hold unlawful and set aside FDA's reclassification action.

38. Under 5 U.S.C. § 706(2)(B), this Court should enjoin FDA from reclassifying Plaintiff's methylphenidate ER tablets in the future without a hearing.

39. Under 28 U.S.C § 2201, this Court should declare FDA's reclassification action unlawful.

Count II
(Direct Right of Action Under the Fifth Amendment)

40. Plaintiff hereby incorporates by reference each and every allegation set forth in paragraphs 1 through 32 above.

41. Plaintiff's ANDA approval for methylphenidate ER tablets is a property right within the meaning of the due process clause of the Fifth Amendment to the U.S. Constitution.

42. FDA's reclassification action deprives Plaintiff of a property right in the ANDA approval for methylphenidate ER tablets.

43. By failing to give Plaintiff a hearing in connection with the reclassification action, FDA has violated Plaintiff's Fifth Amendment due process right to a hearing in connection with deprivation of the property right.

44. Under the Fifth Amendment, this Court should hold unlawful and set aside FDA's reclassification action.

45. Under the Fifth Amendment, this Court should enjoin FDA from reclassifying Plaintiff's methylphenidate ER tablets in the future without a hearing.

46. Under the Fifth Amendment and 28 U.S.C § 2201, this Court should declare FDA's reclassification action unlawful.

Count III
(Agency Action in Excess of Statutory Jurisdiction, Authority, or Limitations, or Short of Statutory Right)

47. Plaintiff hereby incorporates by reference each and every allegation set forth in paragraphs 1 through 32 above.

48. FDA has no statutory authority to take a drug off the market without following the procedures set forth in 21 U.S.C. § 355(e).

49. 21 U.S.C. § 355(e) requires FDA to give a drug's sponsor a hearing in connection with taking a drug off the market. FDA's reclassification action is a final agency action that exceeds FDA's statutory authority by taking a drug off the market without giving the drug's sponsor a hearing as required by 21 U.S.C. § 355(e).

50. 21 U.S.C. § 355(e)(3) requires that for FDA to take a drug off the market for lack of effectiveness, the information and evidence before the agency must establish that there is a lack of substantial evidence that the drug is effective. On information and belief, the information and evidence before the agency does not establish that there is a lack of substantial evidence that Plaintiff's methylphenidate ER tablets are effective. FDA therefore has no statutory authority to take the reclassification action.

51. Under 5 U.S.C. § 706(2)(C), this Court should hold unlawful and set aside FDA's reclassification action.

52. Under 5 U.S.C. § 706(2)(C), this Court should enjoin FDA from reclassifying Plaintiff's methylphenidate ER tablets in the future without a statutory basis for doing so.

53. Under 28 U.S.C § 2201, this Court should declare FDA's reclassification action unlawful.

Count IV
(Agency Action Without
Observance of Procedure Required by Law)

54. Plaintiff hereby incorporates by reference each and every allegation set forth in paragraphs 1 through 32 above.

55. A major premise for FDA's reclassification action is that Plaintiff's methylphenidate ER tablets did not satisfy FDA's new draft guidance for bioequivalence regarding methylphenidate hydrochloride issued on November 6, 2014.

56. FDA's new draft guidance for bioequivalence regarding methylphenidate hydrochloride is a legislative rule and a final agency action. It is a legislative rule, among other things, because it imposes uniform legal limitations regarding drug approval that did not exist before the agency action was taken.

57. Under 5 U.S.C. § 553, FDA was required either to follow notice and comment procedures, or to publish written findings establishing good cause that notice and comment procedures were impracticable, unnecessary, or contrary to the public interest, before issuing the draft guidance and relying upon it to reclassify Plaintiff's drug. However, FDA did neither and thereby violated 5 U.S.C. § 553. Because of this violation of 5 U.S.C. § 553, FDA's issuance of the draft guidance, and reliance upon it to reclassify Plaintiff's drug, constitutes final agency action "without observance of procedure required by law" within the meaning of 5 U.S.C. § 706(2)(D).

58. Under 5 U.S.C. § 706(2)(D), this Court should hold unlawful and set aside both the draft guidance and the reclassification action.

59. Under 5 U.S.C. § 706(2)(D), this Court should enjoin FDA from imposing the draft guidance in the future without following notice and comment procedures.

60. Under 28 U.S.C § 2201, this Court should declare unlawful the draft guidance and the reclassification action.

Count V
(Arbitrary and Capricious Agency Action)

61. Plaintiff hereby incorporates by reference each and every allegation set forth in paragraphs 1 through 32 above.

62. On information and belief, the evidence underlying FDA's action to reclassify Mallinckrodt's methylphenidate ER tablets to Orange Book code BX does not satisfy the evidentiary standard set forth in the Orange Book's description of code BX. FDA's reclassification action is an arbitrary and capricious final agency action within the meaning of 5 U.S.C. § 706(2)(A), because FDA did not follow its own Orange Book procedures in reclassifying the drug.

63. On information and belief, FDA's reclassification action is not the product of reasoned decisionmaking, is not rationally related to the facts, and/or does not account for evidence contrary to its conclusion. FDA's reclassification action is an arbitrary and capricious final agency action within the meaning of 5 U.S.C. § 706(2)(A).

64. Under 5 U.S.C. § 706(2)(A), this Court should hold unlawful and set aside FDA's reclassification action.

65. Under 5 U.S.C. § 706(2)(A), this Court should enjoin FDA from reclassifying Plaintiff's methylphenidate ER tablets in the future without a non-arbitrary basis for doing so.

66. Under 28 U.S.C § 2201, this Court should declare FDA's reclassification action unlawful.

Prayer for Relief

Plaintiff respectfully requests the Court to grant the following relief:

I. Issue an injunction setting aside FDA's actions, and prohibiting its future actions, as described above in paragraphs 37-38, 44-45, 51-52, 58-59 and 64-65;

II. Issue a declaratory judgment declaring that FDA has acted unlawfully as described above in paragraphs 39, 46, 53, 60 and 66; and

III. Award such other relief as this Court deems just and proper.

Respectfully submitted,

/s/ Daniel G. Jarcho

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